

The role of micronutrients in the maintenance of optimum human health

Hilary J Powers
University of Sheffield



The scale of requirements

Vitamins:

water-soluble: B12 folate B1, B2, B6, C, niacin

fat soluble:



Minerals:

iodine iron, zinc, selenium, calcium Na, K, Cl

Central roles in metabolism and human health

Energy metabolism:
B1, B2, B6, niacin, Fe, Cu

Teeth:
A, D, C, Ca

Immune system:
A, Zn, Fe, Se

Reproductive system:
A, E, zinc,

Skin:
A, C, B6, niacin,



Cognition:
folate, B12, zinc

Vision:
A, B2

Neuromuscular:
B vitamins, A

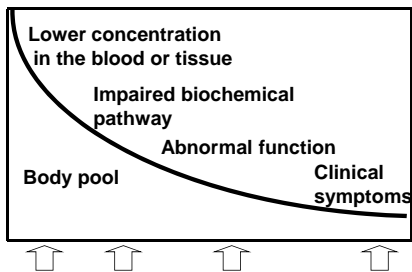
Blood:
K, B2, B6, folate, B12, Fe

skeletal
K, D, C, Ca

Window of adequacy



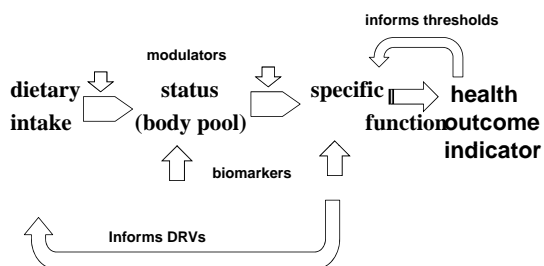
Effects of depletion of the body pool



Criteria for adequacy?

- Avoidance of clinical symptoms of deficiency?
- Maintenance of biochemical markers?
- Saturation of tissue?
- Special benefits?
- Avoidance of toxicity

Setting dietary reference values



Determinants of poor micronutrient status

- **diet**
 - including nutrient/nutrient interactions
- **body stores**
 - fat vs. water soluble
- **rate of turnover**
 - energy requirement, infection, pregnancy
- **malabsorption**
 - gastrointestinal function, gut microbiota,
- **genotype**
 - Eg. polymorphisms in nutrient handling

The global burden of micronutrient deficiency

micronutrient	prevalence (million)
vitamin A*	Pre school 140
	Pregnant women 7
iodine	2000
zinc	2000
iron deficiency anaemia**	4-5000

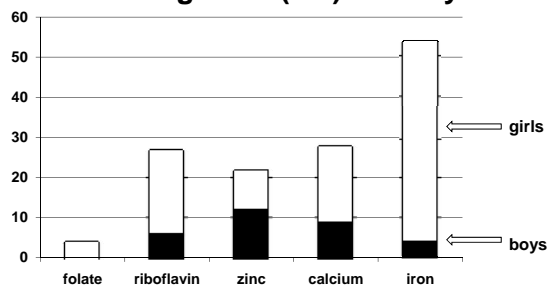
* High risk regions only included

** 'epidemic proportions' (WHO)

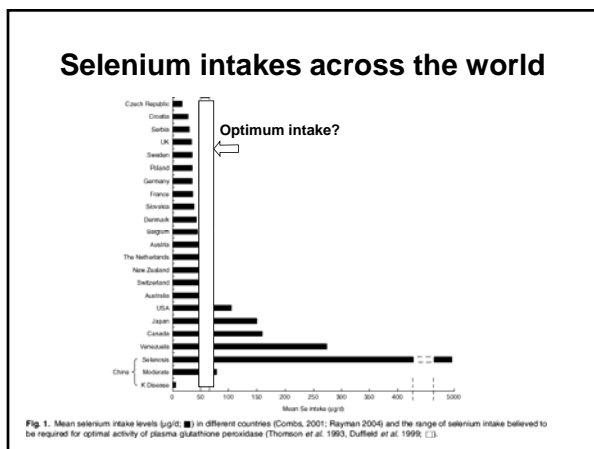
Health implications

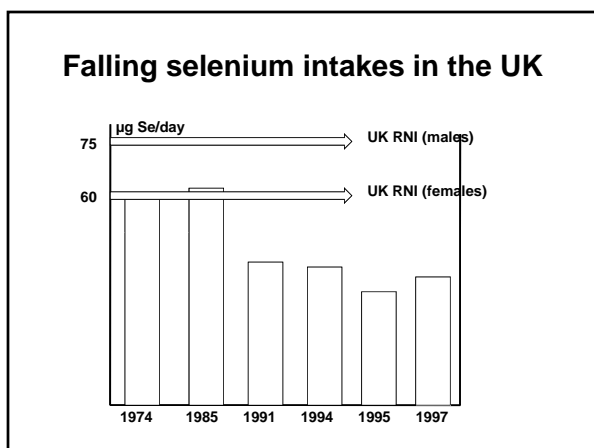
- Vitamin A deficiency → blindness, infection
- Iodine deficiency → poor cognitive development
- Zinc deficiency → impaired growth, infection, stillbirths
- IDA → poor cognitive development, reduced work performance

Not restricted to low income countries eg: Percentage not achieving LRNI (UK): 15-18 yrs



Selenium

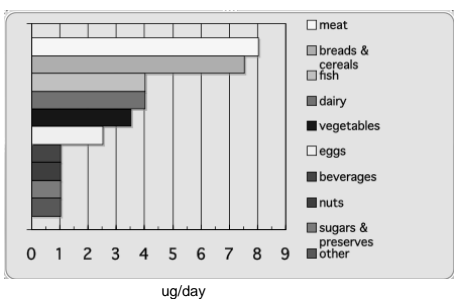




Because...

- Reduced import of US wheat, with high Se content
- Increased use of sulphur fertilizers on crops
- High-grain yields and associated reduced Se concentration (by dilution)
- Reduced combustion of fossil fuels (which generates particulate selenium)

Sources of selenium in the UK diet



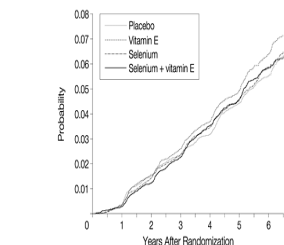
Documented effects of low intakes

- Impaired immune function
- Reduced antioxidant protection
- Impaired fertility
- Cognitive impairment
- Increased cancer risk

Does selenium influence cancer risk?

- Skin cancer
 - NPC trial in men with a history of skin cancer. 200m Se for 4.5years. No significant effect.
- Lung cancer
 - NPC trial: reduced risk in those with lowest baseline status
- Prostate cancer
 - NPC trial: reduced risk in those with lowest baseline status; effect sustained after 2 further years follow-up. Supported by 2 cohort studies.
- Colorectal cancer
 - NPC trial: reduced risk; supported by one cohort

The SELECT trial



Cumulative incidence of prostate cancer according to intervention group.

No protective effect of Se (or vitamin E). Study terminated early.

No. at risk	0	1	2	3	4	5	6
Placebo	8689	8553	8228	8029	7389	4892	2516
Vitamin E	8732	8610	8373	8086	7401	4867	2537
Selenium	8750	8597	8341	8083	7393	4848	2536
Selenium + vitamin E	8700	8585	8371	8097	7428	4894	2580

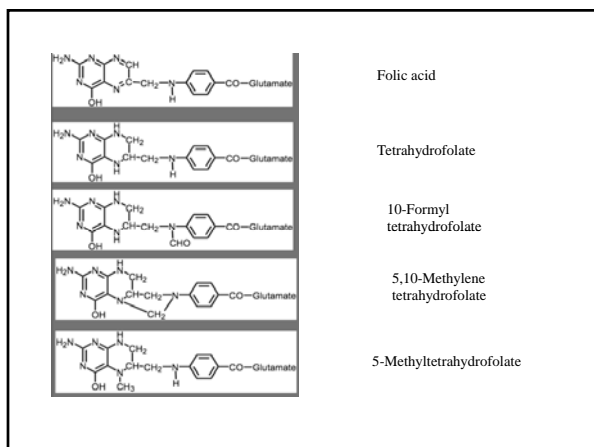
Selenium can be toxic



- NOAEL
 - 15µg/kg body weight
- LOAEL
 - 28µg/kg body weight*
 - Hair loss
 - Nail changes
- Selenosis
 - 90µg/kg body weight
 - Hair loss
 - Skin lesions
 - Nausea and vomiting

LOAEL = 1500µg/day for a 55Kg adult

Folate



Functions of folates

- Synthesis of purines and pyrimidines
- Amino acid metabolism
- Methyl donor (DNA, amino acids, lipids)

Effects of low intakes: megaloblastic anaemia

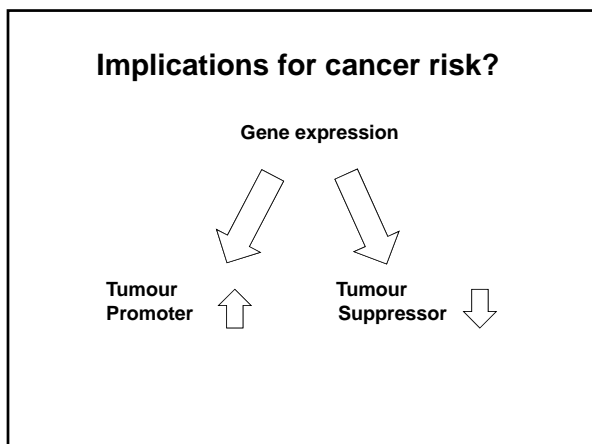
Large red blood cells

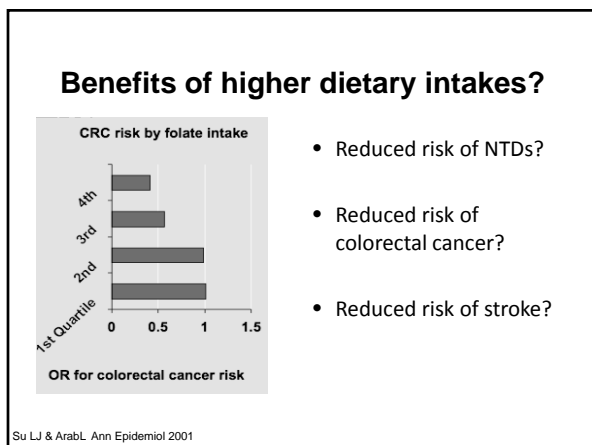
Large neutrophil (white blood cell) with multilobed nucleus

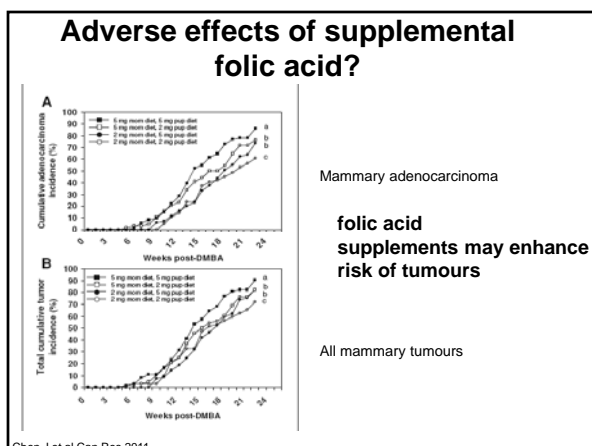
Neural tube defects

Dysregulation of DNA methylation?

1) cystathionine synthase
 2) methionine synthase
 3) 5,10 methylenetetrahydrofolate reductase

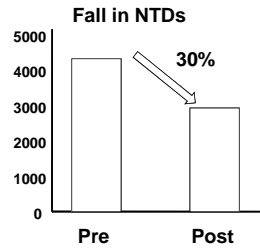






Mandatory fortification of flour with folic acid?

- 300µg folic acid/100g flour
- and
- restrictions on fortification of other foods



Summary

- Micronutrients have key roles in many metabolic processes
- Understanding micronutrient function is central to setting dietary requirements
- Micronutrient status influenced by diet and modulating effects of non-dietary factors
- High intakes may provide special benefits but may also pose risks
